



TGGGCACAGC CACCTGTG GTAGTCCAGG GGCCAGCCCCA CTGAGCTGGC ATATCAGCTG	60
GTGGCCCCGT TGGACTCGGC CCTAGGGAAC GCGGCG ATG GGA GCG CCC CGG ATC	115
Met Gly Ala Pro Arg Ile	5
1	
TGC CAC AGC CTT GCC TTG CTC CTC TGC TGC TCC GTG CTC AGC TCC GTC	163
Ser His Ser Leu Ala Leu Leu Cys Cys Ser Val Leu Ser Ser Val	20
10	
TAC GCA CTG GTG GAT GCC GAT GAT GTC ATA ACG AAG GAG GAG CAG ATC	211
Tyr Ala Leu Val Asp Ala Asp Asp Val Ile Thr Lys Glu Glu Gln Ile	35
25	
ATT CTT CTG CGC AAT GCC CAG GCC CAG TGT GAG CAG CGC CTG AAA GAG	259
Ile Leu Leu Arg Asn Ala Gln Ala Gln Cys Glu Gln Arg Leu Lys Glu	50
40	
GTC CTC AGG GTC CCT GAA CTT GCT GAA TCT GCC AAA GAC TGG ATG TCA	307
Val Leu Arg Val Pro Glu Leu Ala Glu Ser Ala Lys Asp Trp Met Ser	70
55	
AGG TCT GCA AAG ACA AAG AAG GAG AAA CCT GCA GAA AAG CTT TAT CCC	355
Arg Ser Ala Lys Thr Lys Lys Glu Lys Pro Ala Glu Lys Leu Tyr Pro	85
75	
CAG GCA GAG GAG TCC AGG GAA GTT TCT GAC AGG AGC CGG CTG CAG GAT	403
Gln Ala Glu Glu Ser Arg Glu Val Ser Asp Arg Ser Arg Leu Gln Asp	100
90	
GGC TTC TGC CTA CCT GAG TGG GAC AAC ATT GTG TGC TGG CCT GCT GGA	451
Gly Phe Cys Leu Pro Glu Trp Asp Asn Ile Val Cys Trp Pro Ala Gly	115
105	

FIG. 1A

GTG CCC GGC AAG GTG GTG GCC GTG CCC TGC CCC GAC TAC TTC TAC GAC	499
Val Pro Gly Lys Val Val Ala Val Pro Cys Pro Asp Tyr Phe Tyr Asp	
120 125 130	
TTC AAC CAC AAA GGC CGA GCC TAT CGG CGC TGT GAC AGC AAT GGC AGC	547
Phe Asn His Lys Lys Gly Arg Ala Tyr Arg Cys Asp Ser Asn Gly Ser	
135 140 145 150	
TGG GAG CTG GTG CCT GGG AAC AAC CGG ACA TGG GCG AAT TAC AGC GAA	595
Trp Glu Leu Val Pro Gly Asn Asn Arg Thr Trp Ala Asn Tyr Ser Glu	
155 160 165	
TGT GTC AAG TTT CTG ACC AAC GAG ACC CGG GAA CGG GTC TTT GAT	643
Cys Val Lys Phe Leu Thr Asn Glu Thr Arg Glu Arg Glu Val Phe Asp	
170 175 180	
CGC CTC GGA ATG ATC TAC ACT GTG GGC TAC TCC ATC TCT CTG GGC TCC	691
Arg Leu Gly Met Ile Tyr Thr Val Gly Tyr Ser Ile Ser Leu Gly Ser	
185 190 195	
CTC ACT GTG GCT GTG CTG ATT CTG GGT TAC TTT AGG AGG TTA CAT TGC	739
Leu Thr Val Ala Val Leu Ile Leu Gly Tyr Phe Arg Arg Leu His Cys	
200 205 210	
ACC CGA AAC TAC ATT CAC ATG CAT CTC TTC GTG TCC TTT ATG CTC CGG	787
Thr Arg Asn Tyr Ile His Met His Leu Phe Val Ser Phe Met Leu Arg	
215 220 225 230	
GCT GTA AGC ATC TTC ATC AAG GAT GCT GTG CTC TAC TCG GGC GTT TCG	835
Ala Val Ser Ile Phe Ile Lys Asp Ala Val Leu Tyr Ser Gly Val Ser	
235 240 245	

FIG. 1B

ACA GAT GAA ATC GAG CGC ATC ACC GAG GAG GAG CTG AGG GCC TTC ACA	883
Thr Asp Glu Ile Glu Arg Ile Thr Glu Glu Glu Ala Phe Thr	250 255 260
GAG CCT CCC CCT GCT GAC AAG GCG GGT TTT GTG GGC TGC AGA GTG GCG	931
Glu Pro Pro Ala Asp Lys Ala Gly Phe Val Gly Cys Arg Val Ala	265 270 275
GTA ACC GTC TTC CTT TAC TTC CTG ACC ACC AAC TAC TAC TGG ATC CTG	979
Val Thr Val Phe Leu Tyr Phe Leu Thr Thr Asn Tyr Tyr Trp Ile Leu	280 285 290
GTG GAA GGC CTC TAC CTT CAC AGC CTC ATC TTC ATG GCT TTT TTC TCT	1027
Val Glu Gly Leu Tyr Leu His Ser Leu Ile Phe Met Ala Phe Ser	295 300 305 310
GAG AAA AAG TAT CTC TGG GGT TTC ACA TTA TTT GGC TGG GGC CTC CCT	1075
Glu Lys Lys Tyr Leu Trp Gly Phe Thr Leu Phe Gly Trp Gly Leu Pro	315 320 325
GCC GTG TTT GTC GCT GTG TGG GTG ACC GTG AGG GCT ACA CTG GCC AAC	1123
Ala Val Phe Val Ala Val Trp Val Thr Val Arg Ala Thr Leu Ala Asn	330 335 340
ACT GAG TGC TGG GAC CTG AGT TCG GGG AAT AAG AAA TGG ATC ATA CAG	1171
Thr Glu Cys Trp Asp Leu Ser Ser Gly Asn Lys Lys Trp Ile Ile Gln	345 350 355
GTG CCC ATC CTG GCA GCT ATT GTG GTG AAC TTT ATT CTT TTT ATC AAT	1219
Val Pro Ile Leu Ala Ala Ile Val Val Asn Phe Ile Leu Phe Ile Asn	360 365 370

FIG. 1C

ATA ATC AGA GTC CTG GCT ACT AAA CTC CGG GAG ACC AAT GCA GGG AGA Ile Ile Arg Val Leu Ala Thr Lys Leu Arg Glu Thr Asn Ala Gly Arg 375 380 385 390	1267
TGT GAC ACG AGG CAA CAG TAT AGA AAG CTG CTG AAG TCC ACG CTA GTC Cys Asp Thr Arg Gln Gln Phe 395 400	1315
CTC ATG CCG CTA TTT GGG GTG CAC TAC ATC GTC TTC ATG GCC ACG CCG Leu Met Pro Leu Phe 410 415	1363
TAC ACA GAA GTA TCA GGG ATT CTT TGG CAA GTC CAA ATG CAC TAT GAA Tyr Thr Glu Val Ser Gly Ile Leu Trp Gln Val Gln Met His Tyr Glu 425 430	1411
ATG CTC TTC AAT TCA TTC CAG GGA TTT TTC GTT GCC ATT ATA TAC TGT Met Leu Phe Asn Ser Phe Gln Gly Phe 445 450	1459
TTC TGC AAT GGA GAG GTA CAA GCA GAG ATC AAG AAG TCA TGG AGC CGA Phe Cys Asn Gly Glu Val Gln Ala Glu Ile Lys Lys Ser Trp Ser Arg 455 460 465	1507
TGG ACC CTG GCC TTG GAC TTC AAG CGG AAG GCC AGT GGC AGC AGT Trp Thr Leu Ala Leu Asp Phe Lys Arg Lys Ala Arg Ser Gly Ser Ser 475 480 485	1555
ACC TAC AGC TAT GGC CCC ATG GTG TCA CAT ACA AGT GTC ACC AAT GTG Thr Tyr Ser Tyr Gly Pro Met Val Ser His Thr Ser Val Thr Asn Val 490 495 500	1603

FIG. 1D

GGA CCT CGA GGG GGC TGG CCT TGT CCC TCA GCC CTC GAC TAGCTCCTGG	1652
Gly Pro Arg Gly Gly Trp Pro Cys Pro Ser Ala Leu Asp	515
505	
GGCTGGAGCC AGTGCCAATG GCCATCACCA GTTGCCCTGGC TATGTGAAGC ATGGTTCCAT	1712
TTCTGAGAAC TCATTGCCCTT CATCTGGCCC AGAGCCTGGC ACCAAAGATG ACGGGTATCT	1772
CAATGGCTCT GGACTTTATG AGCCAATGGT TGGGGAACAG CCCCTCCAC TCCTGGAGGA	1832
GGAGAGAGAG ACAGTCATGT GACCCATATC	1862

FIG. 1E

TGGGCACAGC CACCCTGTTG GTAGTCCAGG GGCCAGCCCCA CTGAGCTGGC ATATCAGCTG	60
GTGGCCCCGT TGGACTCGGC CCTAGGGAAC GGCGGCG ATG GGA GCG CCC CGG ATC	115
Met Gly Ala Pro Arg Ile	5
TCG CAC AGC CTT GCC TTG CTC CTC TGC TGC TCC GTG CTC AGC TCC GTC	163
Ser His Ser Leu Ala Leu Leu Cys Cys Ser Val Leu Ser Ser Val	20
TAC GCA CTG GTG GAT GCC GAT GAT GTC ATA ACG AAG GAG GAG CAG ATC	211
Tyr Ala Leu Val Asp Ala Asp Val Ile Thr Lys Glu Glu Gln Ile	35
ATT CTT CTG CGC AAT GCC CAG GCC CAG TGT GAG CAG CGC CTG AAA GAG	259
Ile Leu Leu Arg Asn Ala Gln Ala Gln Cys Glu Gln Arg Leu Lys Glu	50
GTC CTC AGG GTC CCT GAA CTT GCT GAA TCT GCC AAA GAC TGG ATG TCA	307
Val Leu Arg Val Pro Glu Leu Ala Glu Ser Ala Lys Asp Trp Met Ser	70
AGG TCT GCA AAG ACA AAG AAG GAG AAA CCT GCA GAA AAG CTT TAT CCC	355
Arg Ser Ala Lys Thr Lys Lys Glu Lys Pro Ala Glu Lys Leu Tyr Pro	85
CAG GCA GAG GAG TCC AGG GAA GTT TCT GAC AGG AGC CGG CTG CAG GAT	403
Gln Ala Glu Glu Ser Arg Glu Val Ser Asp Arg Ser Arg Leu Gln Asp	100
GGC TTC TGC CTA CCT GAG TGG GAC AAC ATT GTG TGC TGG CCT GCT GGA	451
Gly Phe Cys Leu Pro Glu Trp Asp Asn Ile Val Cys Trp Pro Ala Gly	115
GTG CCC GGC AAG GTG GTG GCC GTG CCC TGC CCC GAC TAC TTC TAC GAC	499
Val Pro Gly Lys Val Val Ala Val Pro Cys Pro Asp Tyr Phe Tyr Asp	130

FIG. 2A

TTC AAC CAC AAA GGC CGA GCC TAT CGG CGC TGT GAC AGC AAT GGC AGC	547
Phe Asn His Lys Gly Arg Ala Tyr Arg Arg Cys Asp Ser Asn Gly Ser	135 140 145 150
TGG GAG CTG GTG CCT GGG AAC AAC CGG ACA TGG GCG AAT TAC AGC GAA	595
Trp Glu Leu Val Pro Gly Asn Asn Arg Thr Trp Ala Asn Tyr Ser Glu	155 160 165
TGT GTC AAG TTT CTG ACC AAC GAG ACC CGG GAA CGG GAA GTC TTT GAT	643
Cys Val Lys Phe Leu Thr Asn Glu Thr Arg Glu Arg Glu Val Phe Asp	170 175 180
CGC CTC GGA ATG ATC TAC ACT GTG GGC TAC TCC ATC TCT CTG GGC TCC	691
Arg Leu Gly Met Ile Tyr Thr Val Gly Tyr Ser Ile Ser Leu Gly Ser	185 190 195
CTC ACT GTG GCT GTG CTG ATT CTG GGT TAC TTT AGG AGG TTA CAT TGC	739
Leu Thr Val Ala Val Leu Ile Leu Gly Tyr Phe Arg Arg Leu His Cys	200 205 210
ACC CGA AAC TAC ATT CAC ATG CAT CTC TTC GTG TCC TTT ATG CTC CGG	787
Thr Arg Asn Tyr Ile His Met His Leu Phe Val Ser Phe Met Leu Arg	215 220 225 230
GCT GTA AGC ATC TTC ATC AAG GAT GCT GTG CTC TAC TCG GGG GTT TCC	835
Ala Val Ser Ile Phe Ile Lys Asp Ala Val Leu Tyr Ser Gly Val Ser	235 240 245

FIG. 2B

ACA GAT GAA ATC GAG CGC ATC ACC GAG GAG GAG CTG AGG GCC TTC ACA Thr Asp Glu Ile Glu Arg Ile Thr Glu Glu Glu Arg Ala Phe Thr	883
	250 255 260
GAG CCT CCC GCT GAC AAG GCG GGT TTT GTG GGC TGC AGA GTG GCG Glu Pro Pro Ala Asp Lys Ala Gly Phe Val Gly Cys Arg Val Ala	931
	265 270 275
GTA ACC GTC TTC CTT TAC TTC CTG ACC ACC AAC TAC TAC TGG ATC CTG Val Thr Val Phe Leu Tyr Phe Tyr 285	979
	280 290
GTG GAA GGC CTC TAC CTT CAC AGC CTC ATC TTC ATG GCT TTT TTC TCT Val Glu Gly Leu Tyr Leu His Ser Leu Ile Phe Met Ala Phe Phe Ser	1027
	295 300 305 310
GAG AAA AAG TAT CTC TGG GGT TTC ACA TTA TTT GGC TGG GGC CTC CCT Glu Lys Lys Tyr Leu Tyr 315	1075
	320 325
GCC GTG TTT GTC GCT GTG TGG GTG ACC GTG AGG GCT ACA CTG GCC AAC Ala Val Phe Val Ala Val Trp Val Thr Val Arg Ala Thr Leu Ala Asn	1123
	330 335 340
ACT GAG TGC TGG GAC CTG AGT TCG GGG AAT AAG AAA TGG ATC ATA CAG Thr Glu Cys Trp Asp Leu Ser Ser Gly Asn Lys Lys Trp Ile Ile Gln	1171
	345 350 355
GTG CCC ATC CTG GCA GCT ATT GTG GTG AAC TTT ATT CTT TTT ATC AAT Val Pro Ile Leu Ala Ala Ile Val Val Asn Phe Ile Leu Phe Ile Asn	1219
	360 365 370
ATA ATC AGA GTC CTG GCT ACT AAA CTC CGG GAG ACC AAT GCA GGG AGA Ile Ile Arg Val Leu Ala Thr Lys Leu Arg Glu Thr Asn Ala Gly Arg	1267
	375 380 385 390

FIG. 2C



TGT GAC ACG AGG CAA CAG TAT AGA AAG CTG CTG AAG TCC ACG CTA GTC Cys Asp Thr Arg Gln Gln Arg Lys Leu Leu Thr Leu Val 395 400 405	1315
CTC ATG CCG CTA TTT GGG GTG CAC TAC ATC GTC TTC ATG GCC ACG CCG Leu Met Pro Leu Phe Gly Val His Tyr Ile Val Phe Met Ala Thr Pro 410 415 420	1363
TAC ACA GAA GTA TCA GGG ATT CTT TGG CAA GTC CAA ATG CAC TAT GAA Tyr Thr Glu Val Ser Gly Ile Leu Trp Gln Val Gln Met His Tyr Glu 425 430 435	1411
ATG CTC TTC AAT TCA TTC CAG GGA TTT TTC GTT GCC ATT ATA TAC TGT Met Leu Phe Asn Ser Phe Gln Gly Phe Val Ala Ile Ile Tyr Cys 440 445 450	1459
TTC TGC AAT GGA GAG GTA CAA GCA GAG ATC AAG AAG TCA TGG AGC CGA Phe Cys Asn Gly Glu Val Gln Ala Glu Ile Lys Lys Ser Trp Ser Arg 455 460 465 470	1507
TGG ACC CTG GCC TTG GAC TTC AAG CGG AAG GCC CGG AGT GGC AGC AGT Trp Thr Leu Ala Leu Asp Phe Lys Arg Lys Ala Arg Ser Gly Ser Ser 475 480 485	1555
ACC TAC AGC TAT GGC CCC ATG GTG TCA CAT ACA AGT GTC ACC AAT GTG Thr Tyr Ser Tyr Gly Pro Met Val Ser His Thr Ser Val Thr Asn Val 490 495 500	1603

FIG. 2D

GGA CCT CGA GGG GGG CTG GCC TTG TCC CTC AGC CCT CGA CTA GCT CCT Gly Pro Arg Gly Gly Leu Ala Leu Ser Leu Ser Pro Arg Leu Ala Pro	505 510 515	1651
GGG GCT GGA GCC AGT GCC AAT GGC CAT CAC CAG TTG CCT GGC TAT GTG Gly Ala Gly Ala Ser Ala Asn Gly His His Gln Leu Pro Gly Tyr Val	520 525 530	1699
AAG CAT GGT TCC ATT TCT GAG AAC TCA TTG CCT TCA TCT GGC CCA GAG Lys His Gly Ser Ile Ser Glu Asn Ser Leu Pro Ser Ser Gly Pro Glu	535 540 545	1747
CCT GGC ACC AAA GAT GAC GGG TAT CTC AAT GGC TCT GGA CTT TAT GAG Pro Gly Thr Lys Asp Asp Gly Tyr Leu Asn Gly Ser Gly Leu Tyr Glu	555 560	1795
CCA ATG GTT GGG GAA CAG CCC CCT CCA CTC CTG GAG GAG GAG AGA GAG Pro Met Val Gly Glu Gln Pro Pro Pro Leu Leu Glu Glu Arg Glu	570 575 580	1843
ACA GTC ATG TGACCCATAT C Thr Val Met	585	1863

FIG. 2E

GGGGGGGGCC	GGGGGGGGGA	GCTCGGAGGC	CGGGGGGGGC	TGCCCGGAGG	GACGGGGCCC	60
TAGGCGGTGG	CG	ATG	GGG	GCC	CGG	ATC
	Met	Gly	Ala	Ala	Arg	Ile
	1		5			10
CTA	CTC	TGC	CCA	GTG	CTC	AGC
	Leu	Cys	Pro	Val	Leu	Ser
	15					20
						25
GAC	GAT	GTC	TTT	ACC	AAA	GAG
	Asp	Val	Phe	Thr	Lys	Glu
	30					35
						40
CAG	GCG	CRA	TGT	GAC	AAG	CTG
	Gln	Ala	Gln	Cys	Asp	Lys
	45					50
						55
						60
AAC	ATA	ATG	GAG	TCA	GAC	AAG
	Asn	Ile	Met	Glu	Ser	Asp
						65
						70
						75
AAG	CQC	AGG	AAA	GAG	AAG	GCA
	Lys	Pro	Arg	Lys	Glu	Lys
						80
						85
GAG	AAC	AAG	GAC	GTG	CCC	ACC
	Glu	Asn	Lys	Asp	Val	Pro
						90
						95
						100
CTG	CCC	GAG	TGG	GAC	AAC	ATC
	Leu	Pro	Glu	Trp	Asp	Asn
						110
						115
						120
GAA	GTG	GCA	GTA	CCT	TGT	CCC
	Glu	Val	Val	Ala	Val	Pro
						125
						130
						135
						140

FIG. 3A

AAA GGC CAT GCC TAC AGA CGC TGT GAC CGC AAT GGC AGC TGG GAG GTG Lys Gly His Ala Tyr Arg Arg Cys Asp Arg Asn Gly Ser Trp Glu Val	540
GTT CCA GGG CAC AAC CGG ACG TGG GCC AAC TAC AGC GAG TGC CTC AAG Val Pro Gly His Asn Arg Thr Trp Ala Asn Tyr Ser Glu Cys Leu Lys	588
TTC ATG ACC AAT GAG ACG CGG GAA CGG GAG GTA TTT GAC CGC CTA GGC Phe Met Thr Asn Glu Thr Arg Glu Arg Glu Val Phe Asp Arg Leu Gly	636
ATG ATC TAC ACC GTG GGA TAC TCC ATG TCT CTC GCC TCC CTC ACG GTG Met Ile Tyr Thr Val Gly Tyr Ser Met Ser Leu Ala Ser Leu Thr Val	684
GCT GTG CTC ATC CTG GCC TAT TTT AGG CGG CTG CAC TGC ACG CGC AAC Ala Val Leu Ile Leu Ala Tyr Phe Arg Arg Arg Leu His Cys Thr Arg Asn	732
TAC ATC CAC ATG CAC ATG TTC CTG TCG TTT ATG CTG CGC GCC GCG AGC Tyr Ile His Met His Met Phe Leu Ser Phe Met Leu Arg Ala Ala Ser	780
ATC TTC GTG AAG GAC GCT GTG CTC TAC TCT GGC TTC ACG CTG GAT GAG Ile Phe Val Lys Asp Ala Val Leu Tyr Ser Gly Phe Thr Leu Asp Glu	828

FIG. 3B

GCC GAG CGC CTC ACA GAG GAA GAG TTG CAC ATC ATC GCG CAG GTG CCA Ala Glu Arg Leu Thr Glu Glu Glu Leu His Ile Ile Ala Gln Val Pro 255 260 265	876
CCT CCG CCG GCC GCT GCC GGC GTA GGC TAC GCT GGC TGC CGC GTG GCG Pro Pro Ala Ala Ala Val Gly Tyr Ala Gly Cys Arg Val Ala 270 275 280	924
GTG ACC TTC TTC CTC TAC TTG CAC ACC AAC TAC TAC TGG ATT CTG Val Thr Phe Phe Leu Tyr Phe Leu Ala Thr Asn Tyr Tyr Trp Ile Leu 285 290 295 300	972
GTG GAG GGG CTG TAC TTG CAC AGC CTC ATC TTC ATG GCC TTT TTC TCA Val Glu Gly Leu Tyr Leu His Ser Leu Ile Phe Met Ala Phe Phe Ser 305 310 315	1020
GAG AAG AAG TAC CTG TGG GGC TTC ACC ATC TTC GGC TGG GGT CTA CCG Glu Lys Lys Tyr Leu Trp Gly Phe Thr Ile Phe Gly Trp Gly Leu Pro 320 325 330	1068
GCT GTC-TTC GTG GCT GTG TGG GTC GTC AGA GCA ACC TTG GCC AAC Ala Val Phe Val Ala Val Trp Val Gly Val Arg Ala Thr Leu Ala Asn 335 340 345	1116
ACT GGG TGC TGG GAT CTG AGC TCC GGG CAC AAG AAG TGG ATC ATC CAG Thr Gly Cys Trp Asp Leu Ser Ser Gly His Lys Lys Trp Ile Ile Gln 350 355 360	1164
GTG CCC ATC CTG GCA TCT GTT GTG CTC AAC TTC ATC CTT TTT ATC AAC Val Pro Ile Leu Ala Ser Val Val Leu Asn Phe Ile Leu Phe Ile Asn 365 370 375 380	1212
ATC ATC CCG GTG CTT GCC ACT AAG CTT CGG GAG ACC AAT GCG GGC CGG Ile Ile Arg Val Leu Ala Thr Lys Leu Arg Glu Thr Asn Ala Gly Arg 385 390 395	1260

FIG. 3C

TGT GAC ACC AGG CAG CAG TAC CGG AAG CTG CTC AGG TCC ACG TTG GTG	1308
Cys Asp Thr Arg Gln Gln Tyr Arg Lys Leu Leu Ser Thr Leu Val	400 405 410
CTC GTG CCG CTC TTT GGT GTC CAC TAC ACC GTC TTC ATG GCC TTG CCG	1356
Leu Val Pro Leu Phe Gly Val His Tyr Thr Val Phe Met Ala Leu Pro	415 420 425
TAC ACC GAG GTC TCA GGG ACA TTG TGG CAG ATC CAG ATG CAT TAT GAG	1404
Tyr Thr Glu Val Ser Gly Thr Leu Trp Gln Ile Gln Met His Tyr Glu	430 435 440
ATG CTC TTC AAC TCC TTC CAG GGA TTT TTT GTT GCC ATC ATA TAC TGT	1452
Met Leu Phe Asn Ser Phe Gln Gly Phe Phe Val Ala Ile Ile Tyr Cys	445 450 455 460
TTC TGC AAT GGT GAG GTG CAG GCA GAG ATT AGG AAG TCA TGG AGC CGC	1500
Phe Cys Asn Gly Glu Val Gln Ala Glu Ile Arg Lys Ser Trp Ser Arg	465 470 475
TGG ACA CTG GCG TTG GAC TTC AAG CGC AAA GCA CGA AGT GGG AGT AGC	1548
Trp Thr Leu Ala Leu Asp Phe Lys Arg Lys Ala Arg Ser Gly Ser Ser	480 485 490
AGC TAC AGC TAT GGC CCA ATG GTG TCT CAC ACG AGT GTG ACC AAT GTG	1596
Ser Tyr Ser Tyr Gly Pro Met Val Ser His Thr Ser Val Thr Asn Val	495 500 505

FIG. 3D

GGC CCC CGT GCA GGA CTC AGC CTC CCC CTC AGC CCC CGC CTG CCT CCT CCT	1644
Gly Pro Arg Ala Gly Leu Ser Leu Pro Leu Ser Pro Arg Leu Pro Pro	
510 515 520	
GGC ACT ACC AAT GGC CAC TCC CAG CTG CCT GGC CAT GCC AAG CCA GGG	1692
Ala Thr Thr Asn Gly His Ser Gln Leu Pro Gly His Ala Lys Pro Gly	
525 530 535	
GCT CCA GCC ACT GAG ACT GAA ACC CTA CCA GTC ACT ATG GCG GTT CCC	1740
Ala Pro Ala Thr Glu Thr Glu Thr Leu Pro Val Thr Met Ala Val Pro	
545 550 555	
AAG GAC GAT GGA TTC CTT AAC GGC TCC TGC TCA GGC CTG GAT GAG GAG	1788
Lys Asp Asp Gly Phe Leu Asn Gly Ser Cys Ser Gly Leu Asp Glu Glu	
560 565 570	
GCC TCC GGG TCT GCG CCG CCT CCA TTG TTG CAG GAA GGA TGG GAA	1836
Ala Ser Gly Ser Ala Arg Pro Pro Pro Leu Leu Gln Glu Gly Trp Glu	
575 580 585	
ACA GTC ATG TGA CTGGGCA CTAGGGGGCT AGACTGCTGG CCTGGGCACA	1885
Thr Val Met	
590	
TGGACAGATG GACCAAGAAG CCAGTGTTC GCTGGTTGTC TATTCGGGAT CTGGACCAGG	1945
AAGATAACAA AAGGAAAATG GAAGTGGACG AAGCAGAGAA GAAGGAAGAG GTTTTCAGG	2005
AATTAAATAT GTTTCCTCAG TTGGATGATG AGGACACAAG GAAGGC	2051

FIG. 3E

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1  MGAARIAPSLALLLCCPVLSAYALVDADDVFTKKEEQIFLLHRAQAQCDK  50
| | | | | . . . . . | | | | | . . . . . | | | | | . . . . .
1  MGAPRISHSLALLLCCSVLSSVYALVDADDVITKKEEQIILLRNAQAQCEQ  50

51  LLKEVLHTAANIMESDKGWTPASTSGKPRKEKASCKFYFESKENKDVPTG  100
| | | | | : . : : | | . : | | : | . : | | : . : | | : . : | | .
51  RLKEVLR.VPELAESAKDW..MSRSAKTKEKPAEKLYPQAEESREVS DR  97

101  SRRRGRPCLPEDWNIVCWPLGAPGEVVAVPCPDYIYDFNHKGHAYRRCDR  150
| | . : | | | | | | | | | | . | | . | | | | | | | | | | | | | | | |
98  SRLQDGFCLPEWDNIVCWPA GVP GKVVAVPCPDYFYDFNHKGGRAYRCD S  147

151  NGSWEVVPGHNR TWANYSECLKFMTNETREREVFDR LGMIYTVGYSMSLA  200
| | | | | : | | : | | | | | | | : | | : | | | | | | | | | | | | | |
148  NGSWELVPGNNR TWANYSECVKFLTNETREREVFDR LGMIYTVGY SISLG  197

201  SLTVAVLILAYFRRLHCT RNYIHMHMF LSFMLRAASIFVKDAVLYSGFTL  250
| | | | | : | | | | | | | | | | : | | | | | . | | : | | | | | . .
198  SLTVAVLILGYFRRLHCT RNYIHMHLFV SFMLRAVSIFIKDAVLYSGVST  247

251  DEAERLTEEELHIIAQVPPPPAAAAVG YAGCRVAVTFFLYFLATNYYWIL  300
| | | | : | | | | : . : . | | : | . . : . | | | | | . | | | | |
248  DEIERITEEELRAFTE...PPPADKAGFVGCRVAVTVFLYFLT TNYWIL  294

301  VEGLYLHSLIFMAFFSEKKYLWGFTIFGWGLPAV FVAVVWGV RATLANTG  350
| | | | | : | | | | | | | | | | : | | | | | | | | | | . | | | | | :
295  VEGLYLHSLIFMAFFSEKKYLWGFTLFGWGLPAV FVAVVWTV RATLANTE  344

351  CWDLSSGHKKWIIQVPILASVVLNFI LFINIIRVLATKLRETNAGRC DTR  400
| | | | | : | | | | | | | | | | . : | | | | | | | | | | | | | | |
345  CWDLSSGNKKWIIQVPILAAIVVNFI LFINIIRVLATKLRETNAGRC DTR  394

401  QQYRKLLRSTLVLP LFGVHYTVFMALPYTEVSGTLWQIQMHYEMLFNSF  450
| | | | | : | | | | | : | | | | | . | | | | | | | | : | | | | |
395  QQYRKLLKSTLVLMPLFGVHYIVFMATPYTEVSGILWQVQMHYEMLFNSF  444

451  QGFFVAIIYCF CNGEVQAEIRKSWSRWTLALDFKRKARSGSSSYSGPMV  500
| | | | | | | | | | | | | | | : | | | | | | | | | | | | | | | |
445  QGFFVAIIYCF CNGEVQAEIKKSWSRWTLALDFKRKARSGSSTYSYSGPMV  494

501  SHTSVTNVGP RAGLSLPLSPRLPP...ATTNGHSQ LPHAKPGAPATETE  547
| | | | | | | | : | | . | | | | : | | . . | | | | | . | | . . . :
495  SHTSVTNVGP RGLALSLSPLAPGAGASANGMHQLPGYVKHGSISENSL  544

548  TLPVTMAVPKDDGFLNGSCSGLDEEASGSARPPPLLQEGWETVM  591
. . . . . : | | | | : | | | | | | | | | | . | | | | | : | | | |
545  PSSGPEPGTKDDGYLNG..SGLYEPMVG.EOPPP LLEEERETVM  585

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Gap Weight:	3.000	Average Match:	0.540
Length Weight:	0.100	Average Mismatch:	-0.396
Quality:	712.2	Length:	594
Ratio:	1.215	Gaps:	6
Percent Similarity:	87.113	Percent Identity:	77.835

FIG. 4



Page 17 of 36  
 Appl. No.: 09/199,874  
 Amendment in Reply to Office action of August 5, 2004  
 Replacement Sheet

						*
R15	MGAARIAPSL	ALLLCCPVLS	SAYALVDADD	VFTKEEQIFL	LHRAQAQCDK	50
Okh	MGAPRISHSL	ALLLCCSVLS	SVYALVDADD	VITKEEQIIL	LRNAQAQCEQ	50
Okh	MGAPRISHSL	ALLLCCSVLS	SVYALVDADD	VITKEEQIIL	LRNAQAQCEQ	50
	----- A -----					
R15	LLKEVLHTAA	NIMESDKGWT	PASTSGKPRK	EKASGKFYPE	SKENKDVPTC	100
Okh	RLKEVLR.VP	ELAESAQDW.	.MSRSAKTKK	EKPAEKLYPQ	AEESREVSDR	97
Okh	RLKEVLR.VP	ELAESAQDW.	.MSRSAKTKK	EKPAEKLYPQ	AEESREVSDR	97
R15	SRRRGRPCLP	EWDNIVCWPL	GAPGEVVAVP	CPDYIYDFNH	KGHAYRRCDR	150
Okh	SRLQDGFCLP	EWDINVCWPA	GVPKGKVVAVP	CPDYFYDFNH	KGRAYRRCDR	147
Okh	SRLQDGFCLP	EWDNIVCWPA	GVPKGKVVAVP	CPDYFYDFNH	KGRAYRRCDR	147
	----- B -----					
R15	NGSWEVVPKH	NRTWANYSEC	LKFMTNETRE	REVFDRGLMI	YTVGYSMSLA	200
Okh	NGSWELVPGN	NRTWANYSEC	VKFLTNETRE	REVFDRGLMI	YTVGYSSISLG	197
Okh	NGSWELVPGN	NRTWANYSEC	VKFLTNETRE	REVFDRGLMI	YTVGYSSISLG	197
	----- C -----					
R15	SLTVAVLILA	YFRRHLHCTR	YIHMHLFVSF	MLRAASIFVK	DAVLYSGFTL	250
Okh	SLTVAVLILG	YFRRHLHCTR	YIHMHLFVSF	MLRAVSIFIK	DAVLYSGVST	247
Okh	SLTVAVLILG	YFRRHLHCTR	YIHMHLFVSF	MLRAVSIFIK	DAVLYSGVST	247
	----- D -----					
R15	DEAERLTEEE	LHIIAQVPPP	PAAAVGYAG	CRVAVTFFLY	FLATNYYWIL	300
Okh	DEIERITEEE	LRAFTE...P	PPADKAGFVG	CRVAVTVFLY	FLTTNYYWIL	294
Okh	DEIERITEEE	LRAFLT...P	PPADKAGFVG	CRVAVTVFLY	FLTTNYYWIL	294
	----- E -----					
R15	VEGLYLHSLI	FMAFFSEKKY	LWGFTLFGWG	LPAVFVAVVW	GVRATLANTG	350
Okh	VEGLYLHSLI	FMAFFSEKKY	LWGFTLFGWG	LPAVFVAVVW	TVRATLANTE	344
Okh	VEGLYLHSLI	FMAFFSEKKY	LWGFTLFGWG	LPAVFVAVVW	TVRATLANTE	344
	----- F -----					
R15	CWDLSSGHKK	WIIQVPILAS	VVLNFIIFIN	IIRVLATKLR	ETNAGRCDTR	400
Okh	CWDLSSGNKK	WIIQVPILAA	IVVNFILFIN	IIRVLATKLR	ETNAGRCDTR	394
Okh	CWDLSSGNKK	WIIQVPILAA	IVVNFILFIN	IIRVLATKLR	ETNAGRCDTR	394
	----- H -----					
R15	QQYRKLLRST	LVLVPLFGVH	YTVFMALPYT	EVSGTGWQIQ	MHYEMLFNSF	450
Okh	QQYRKLLKST	LVLMLPLFGVH	YIVFMATPYT	EVSGILWQVQ	MHYEMLFNSF	444
Okh	QQYRKLLKST	LVLMLPLFGVH	YIVFMATPYT	EVSGILWQVQ	MHYEMLFNSF	444
	----- I -----					
R15	QGFVVAIIYC	FCNGEVQAEI	RKSWSRWTLA	LDFKRKARSG	SSSYSYGPMV	500
Okh	QGFVVAIIYC	FCNGEVQAEI	KKSWSRWTLA	LDFKRKARSG	SSTYSYGPMV	494
Okh	QGFVVAIIYC	FCNGEVQAEI	KKSWSRWTLA	LDFKRKARSG	SSTYSYGPMV	494
	----- J -----					
R15	SHTSVTNVGP	RAGLSLPLSP	RLPP...ATT	NGHSQLPGHA	KPGAPATETE	547
Okh	SHTSVTNVGP	RGGLALSLSL	RLAPGAGASA	NGHHQLPGYV	KHGSISENSL	544
Okh	SHTSVTNVGP	RGG.....	....WPCPSA	LD		515
R15	TLPVTMAVPK	DDGFLNGSCS	GLDEEASGSA	RPPPLLQEGW	ETVM	591
Okh	PSSGPEPGTK	DDGYLNG..S	GLYEPVME.E	QPPPLLEER	ETVM	585

FIG. 5

With I enzymes: SACI

```

2      GGGATCCCGCGCCCTAGCGGTGGCGatgggACCCCGgatcgaccccgctggcg
61      -----
      CCTAGGCGCGCGGATCCGCCACCGctacccCTggCGggcctagcgtggcgccgacccg
      -
      M G T A R I A P G L A
      -
62      ctccctgctgctgccccgtgctcagctccgcgctacgcgctggtggatgcagatgacgtc
121      -----
      gaggacgagacgacggggcacgagtcgaggcgcatgcgcgaccacctacgtctactgcag
      -
      L L L C C P V L S S A Y A L V D A D D V
      -
122      atgactaaagaggaacagatcttccctgctgcaccgtgctcagggcccgagtcgcgaaaaacgg
181      -----
      tactgatttctccttgctctagaaggacgacctttcacgagtcgggtcacgctttttgcc
      -
      M T K E E Q I F L L H R A Q A Q C E K R
      -
182      ctcaaggaggctcctgcagaggccagccagcataatggaatcagacaagggatggacatct
241      -----
      gatttcctccaggacgtctccggtcggtcggtattaccttagtctgttccctacctgtaga
      -
      L K E V L Q R P A S I M E S D K G W T S
      -
242      gcgtccacatcaggggaagcccgaaagataaggcatcttggaagctctaccctgagtct
301      -----
      cgcagggtgtagtcccttagggctccttctattccgtagacccttcgagatgggactcaga
      -
      A S T S G K P R K D K A S G K L Y P E S
      -

```

FIG. 6A

```
302 gagaggaaggagcaccactggcagcaggaaccgagggccccctgtctgccgga  
-----  
361 ctccctcctgttcctccgtgggtgacctcctcctccatggctcccggggacagacggcctt  
-----  
E E D K E A P T G S - . R G R P C L P E -  
-----  
362 tgggaccacatcctgtgctggccgctggggcaccagggtgaggtgggtgtgccctgt  
-----  
421 accctgggtgtaggacacgacggcgaccccccgctgggtccactccaccacggacacgggaca  
-----  
W D H I L C W P L G A P G E V V A V P C -  
-----  
422 ccggactacatttatgacttcaatcacaaaggccatgcctaccgacgctgtgaccgcaat  
-----  
481 ggccctgatgtaaatactgaagttagtgtttccggtacggatggctgcgacactggcgctta  
-----  
P D Y I Y D F N H K G H A Y R R C D R N -  
-----  
482 ggcagctgggagctgggtgcctgggcacacaggaacgtgggccaactacagcagtggtgc  
-----  
541 ccgtcacccctcgaccacggaacccgtgtgtcctgcaccccggttgatgtcgctcacacag
```

FIG. 6B

542 G S W E L V P G H N R T W A N Y S E C V -  
aaatttctcaccacgagactcgtgaacgggaggtgttgaccgcctgggcattttac  
-----  
601 tttaagagtgttactctgagcacttgccctccacaaactggcgaccgtactaaatg  
K F L T N E T R E R E V F D R L G M I Y -  
accgtgggtactccgtgtccctggcgctccctcaccgtagctgtgctcatcctggcctac  
-----  
661 tggcaccggatgaggcacaggacggcaggagtggtgcatcgacacgagtaggacccgatg  
T V G Y S V S L A S L T V A V L I L A Y -  
tttaggggtgactgcacgcgcaactacatccacatgcacctgttctcttccttcctg  
-----  
721 aaatccgcgcgacgtgacgtgcgcgttgatgtaggtgtacgtggacaaggacaggaagtac  
F R R L H C T R N Y I H M H L F L S F M -  
ctgcgcgcgcgtgagcatcttctgtaaggacgctgtgctctactctggtgcgcacgcttgat  
-----  
781 gacgcgcgcactcgtagaagcagttcctgcgcacgagatgagaccgcggtgcgaacta  
L R A V S I F V K D A V L Y S G A T L D -

FIG. 6C

782 gaggtgagcgctcaccgaggaggagctgcgcgccatgccccaggcgccccgcgcgct  
-----  
841 ctccgactcgggagtggtcctcctcctcgcgcgcggtagcgggtccgcgggcgcgga  
-----  
- E A E R L T E E E L R A I A Q A P P P P  
-----  
842 gccaccgcgctgcgcggtacgcggggtccagggtggtgtgaccttcttcttacttc  
-----  
901 cggtggcggcgacggccgatgcgcgcgacgtcccaccgacactggaagaaggaaatgaag  
-----  
- A T A A A G Y A G C R V A V T F F L Y F  
-----  
902 ctggccaccaactactaggattctggtggagggtgtacctgcacagcctcatcttc  
-----  
961 gaccggtggtgatgatgacctaagaccacacctcccgcacatggacgtgttgagtagaag  
-----  
- L A T N Y Y W I L V E G L Y L H G L I F  
-----  
1021 atggccttctcagagaagaagtacctgtggggttcacagtcttcggtggtgctg  
-----  
taccggaagaagagtctcttcttcattgacaccccgaaagtgtcagaagccgacccagac  
-----  
- M A F F S E K K Y L W G F T V F G W G L  
-----  
1022 cccgctgtcttcggtggtgtggtcagtgatcagagctacctggcccaacccgggtgc  
-----  
999gcacagaagcaccgcacacacccagtcacagtctcgatgggaccggtgtgccccacg  
-----  
- P A V F V A V W V S Y R A T L A N T G C  
-----

FIG. 6D

S  
a  
c

1082	tgggacttgagctccgggaacaaaagtggatcatccaggtgcccatcctggcctccatt	1141
	-----	
	accctgaactcgagggcccttggtttcacctagcaggtccacgggtaggaccggaggttaa	
	W D L S G G N K K W I I Q V P I L A S I	-
	gtgctcaacttcacctcttcatcaatatcgctccgggtgctcgccaccaagcagcgggag	1201
1142	-----	
	cacgagttgaagtaggagaagtagttatagcagggccacgagcggtggttcgtcgccctc	
	V L N F I L F I N I V R V L A T K Q R E	-
	accaaagccggccgggtgtgacacacggcagcagtagtaccgggaagctgctcaaatccacgctg	1261
1202	-----	
	tggttgccggccgacactgtgtgcccgtcgctcatggccttcgacgagtttaggtgcgac	
	T N A G R C D T R Q Q Y R K L L K S T L	-
	gtgctcatgcccctcttggcgccactacattgtcttcatggccacaccatacacccgag	1321
1262	-----	
	cacgagtacggggagaaaaccgcaggtgatgtaacagaagtagcgggtgtggtatgtggctc	
	V L M P L F G V H Y I V F M A T P Y T E	-
	gtctcaggacgctctggcaagtcagatgcactatgagatgctcttcaactccttccag	1381
1322	-----	
	cagagtcctcgagaccgttcagggtctacgtcatactctacgagaagttgaggaaggtc	
	V S G T L W Q V Q M H Y E M L F N S F Q	-

FIG. 6E

1382 ggattttttgtcgcaatcatataactgtttctgcaatggcgagggtacaagctgagatcaag  
-----  
cctaaaaaacagcggttagtatatgacaaagacggttaccgctccatggttcgactctagttc  
-----  
1441 G F F V A I I Y C F C N G E V Q A E I K  
-----  
1442 aaatcttgagccgctggacactggcactggcacttcaagcgaagcagcagcgggagc  
-----  
1501 tttagaacctcggcgacctgtgacctgacgtgaagtgcgttccgagcgtcgccctcg  
-----  
K S W S R W T L A L I F K R K A R S G S  
-----  
1502 agcagctatagctacggcccatggtgtccacacaaagtgtgaccaaagtgcggcccccgt  
-----  
1561 tegtatatatgatgcggggtaccacaggggtgtgtcacactggttacagccgggggca  
-----  
S S Y S Y G P M V S H P S V T N V G P R  
-----  
1562 gtgggactcggcctgcccctcagccccgcctactgccactgccaccaccaagccac  
-----  
caccctgagccgacgggagtcggggcggtgacgggtgacgggtggtggtggtggtg  
-----  
V G L G L P L S P R L L P T A T T N G H  
-----  
1621 cctcagctgcctggccatgccaagccagggaccgccccagccctggagaccctcgagaccaca  
-----  
1681 ggagtcgacggaccggtacggttcggtccctgggtcgggacacctctgggagctctggtgt  
-----  
P Q L P G H A K P G T P A L E T L E T T

FIG. 6F

```
1682      ccacctgttatggctgctcccaaggacgatgggttcctcaacggctcctgctcaggcctg
-----
1741      ggtggacggtaccgaccagggttcctgctacccaaggagtgtccgaggacgagtcceggac
-----
      P P A M A A P K D D G F L N G S C S G L
      -
1742      gacgaggagcctctggcctgagcggccacctgccctgctacaggaagatgggagaca
-----
1801      ctgctcctcggagaccggactcgcgggtggacgggacgatgtccttctcacccctctgt
-----
      D E E A S F P E R P A L L Q E E W E T
      -
1802      gtcatgtgaccaggcgctggggctggacctgctgacatagtggatggacagatggacca
-----
1861      cagtacactggtccgcgacccccgcacctggacgactgtatcacctacctgtctacctggt
-----
      V M
1862      aaagatgggtggtgaatgatttcccactcaggcctggggccaaagagaaaaaacaggg
-----
1921      ttctaccaccaacttactaaagggtgagtcceggaccccggttctcctttttgtccc
-----
1922      gaaaaaagaaaaaaagaaaaagaaaaaaagaaaaaaagaaaaaaagaaaaaa
-----
1981      ctttttctctttttttctctttttctctttttttttttttttttttttttttttt
-----
1982      aaaaaaaagaaaaaaagaaaaaaagaaaaaaagaaaaaaagaaaaaaagaaaaaa
-----
      ----- 2011
      tttttttttttttttttttttttttttttttttttttttttttttttttttttt
```

FIG. 6G

Enzymes that do cut:

SacI



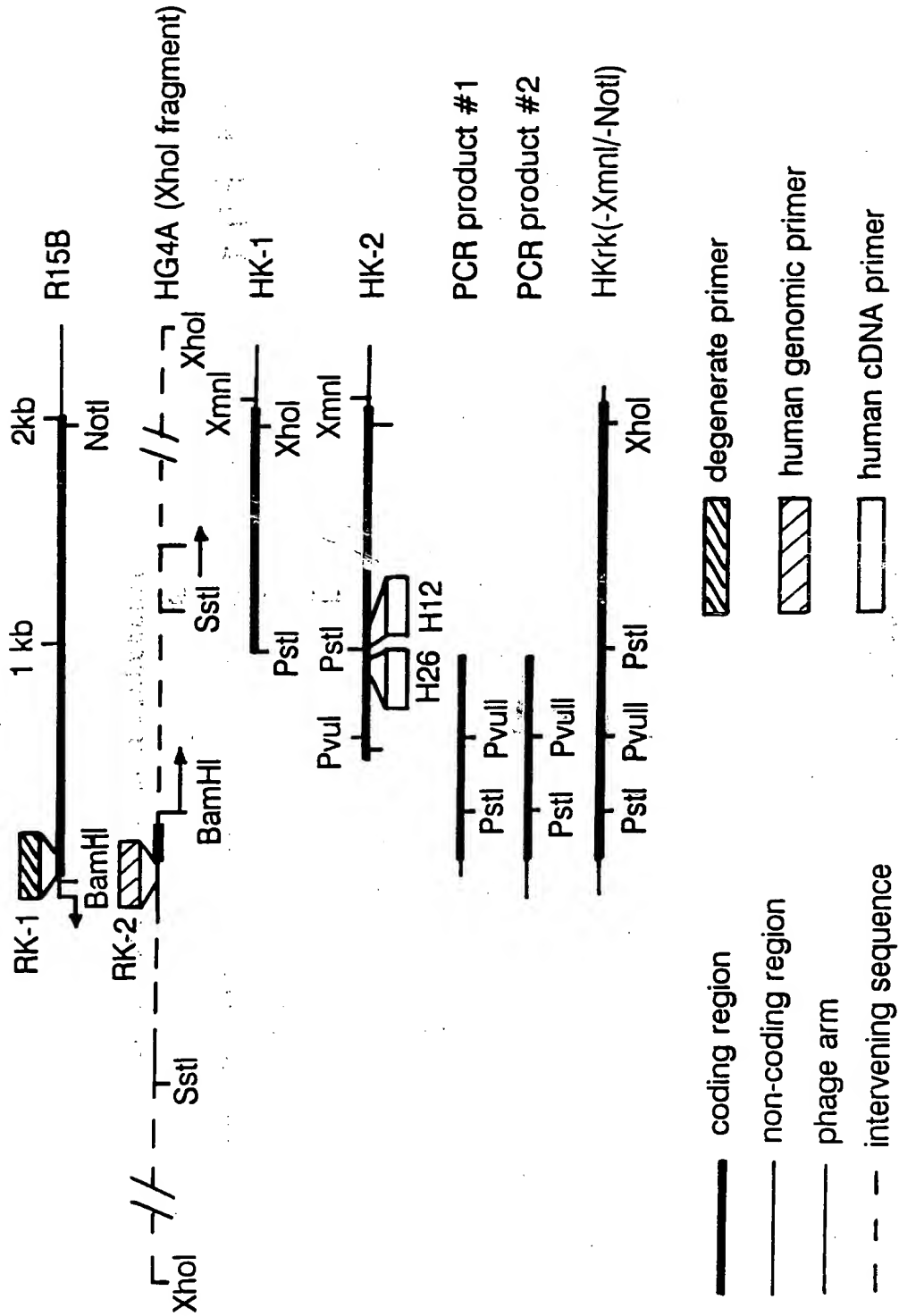


FIG. 7

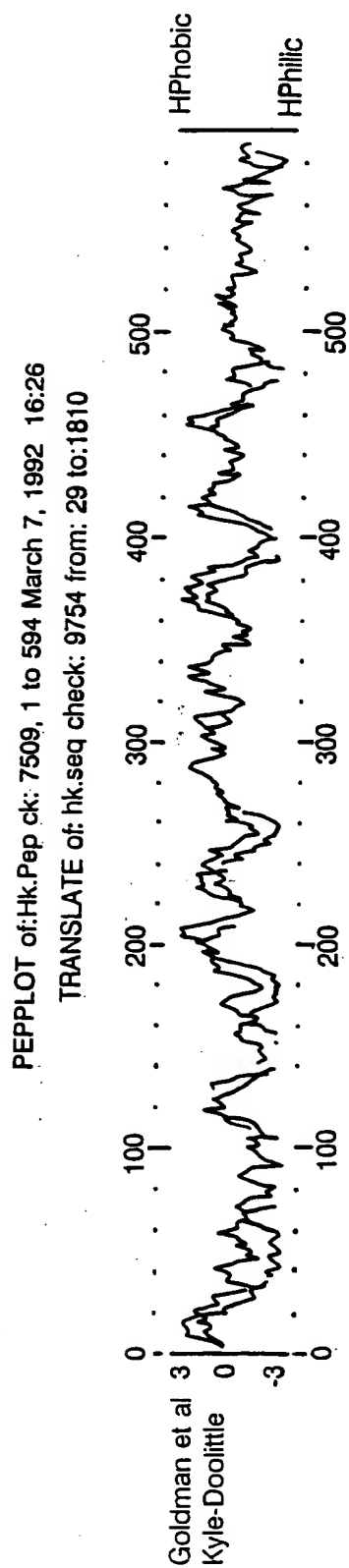


FIG. 8

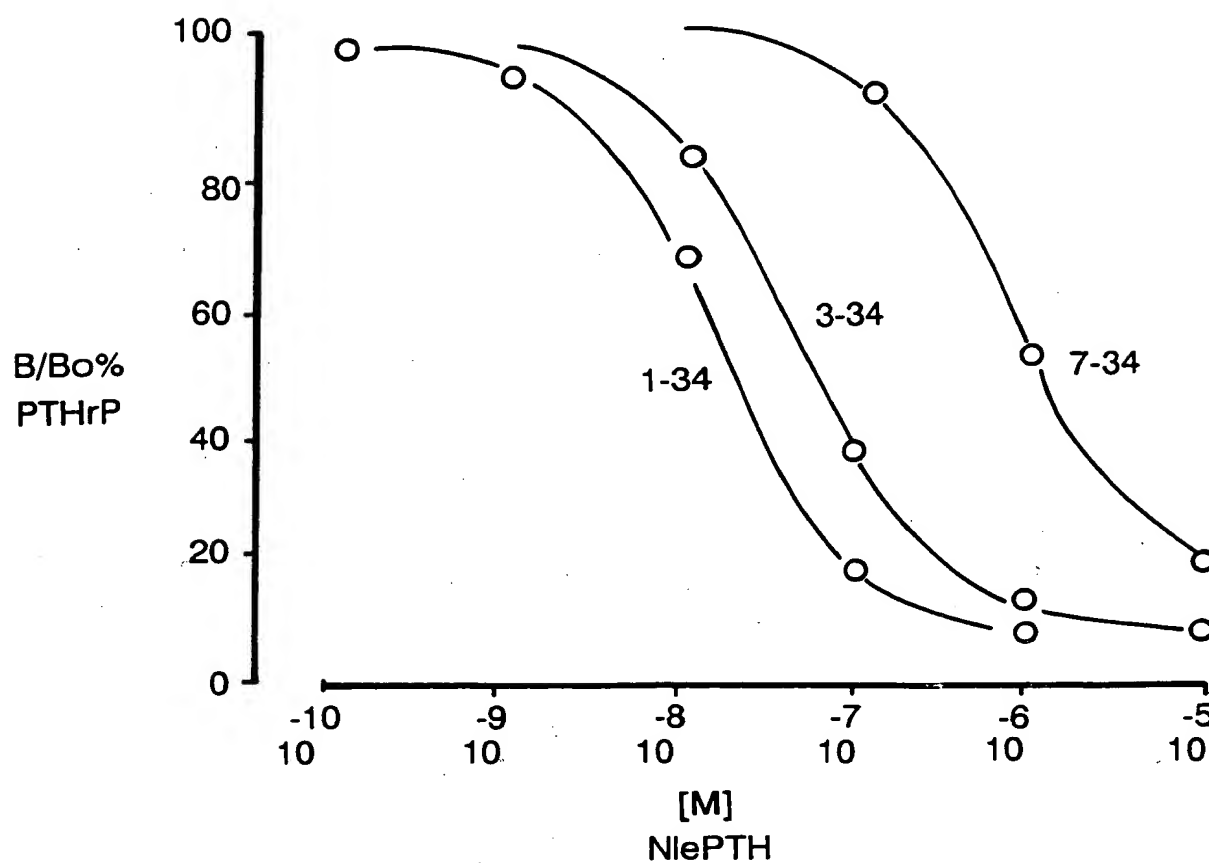


FIG. 9

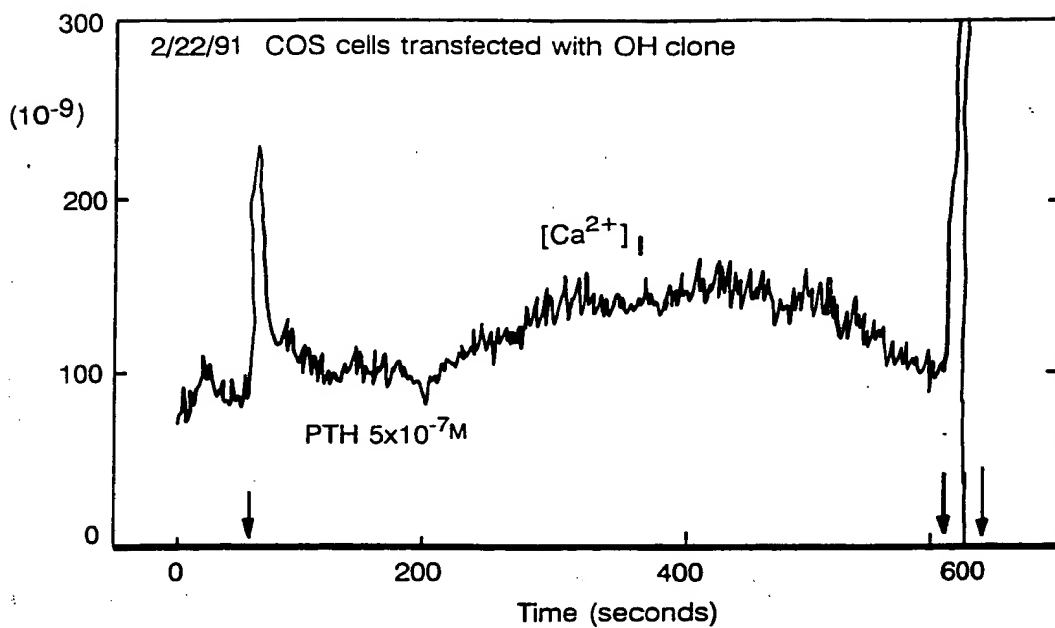


FIG. 10

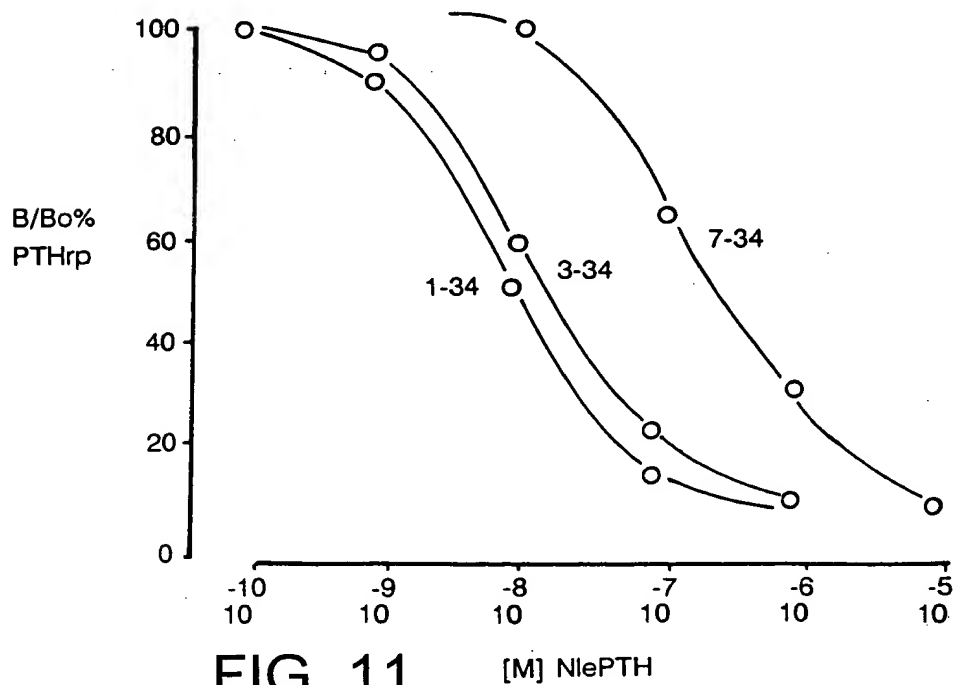


FIG. 11

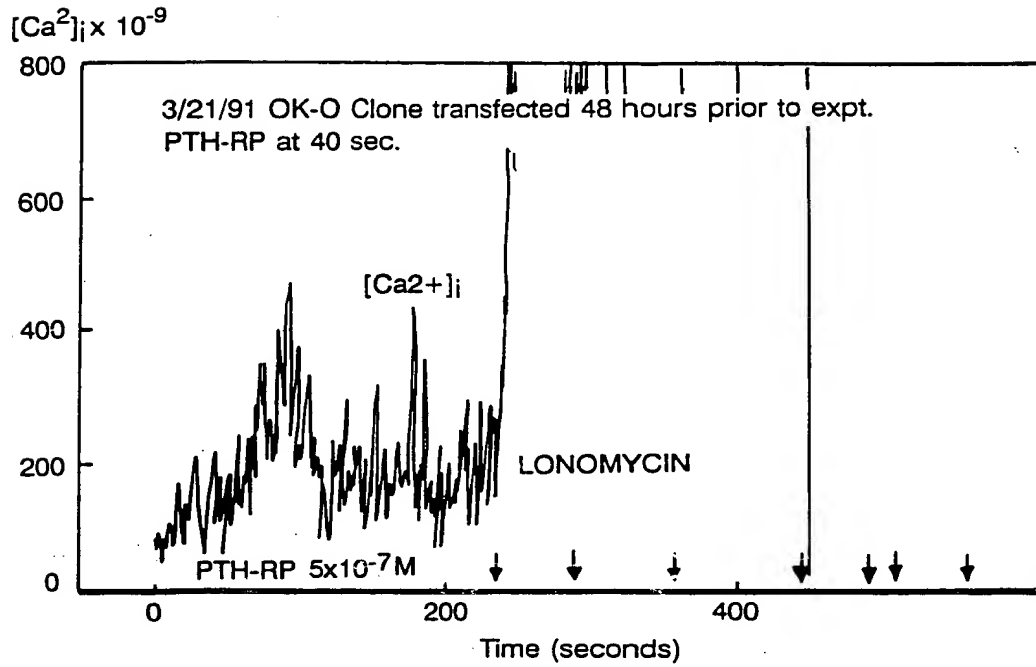


FIG. 12

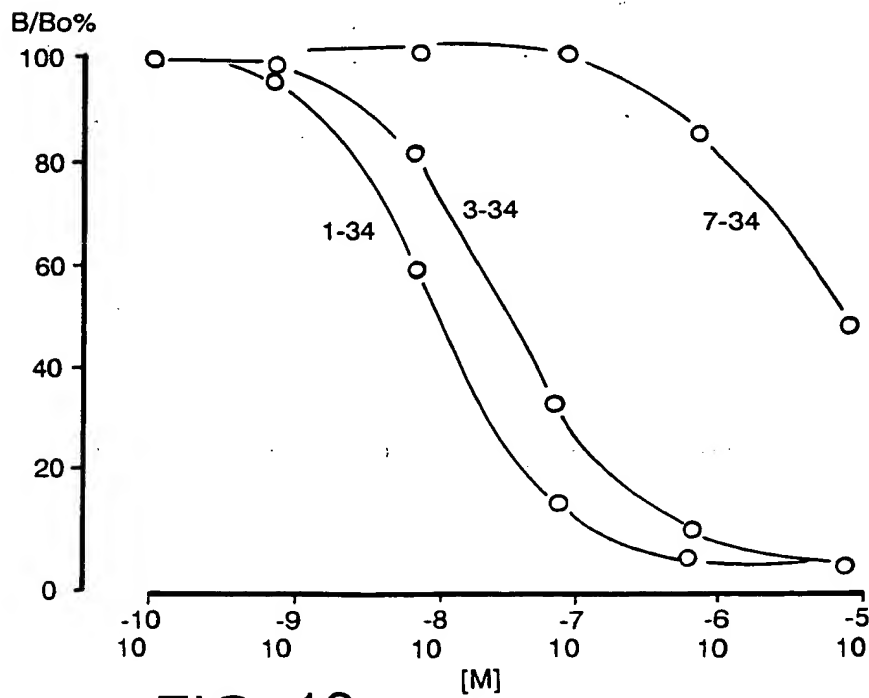


FIG. 13

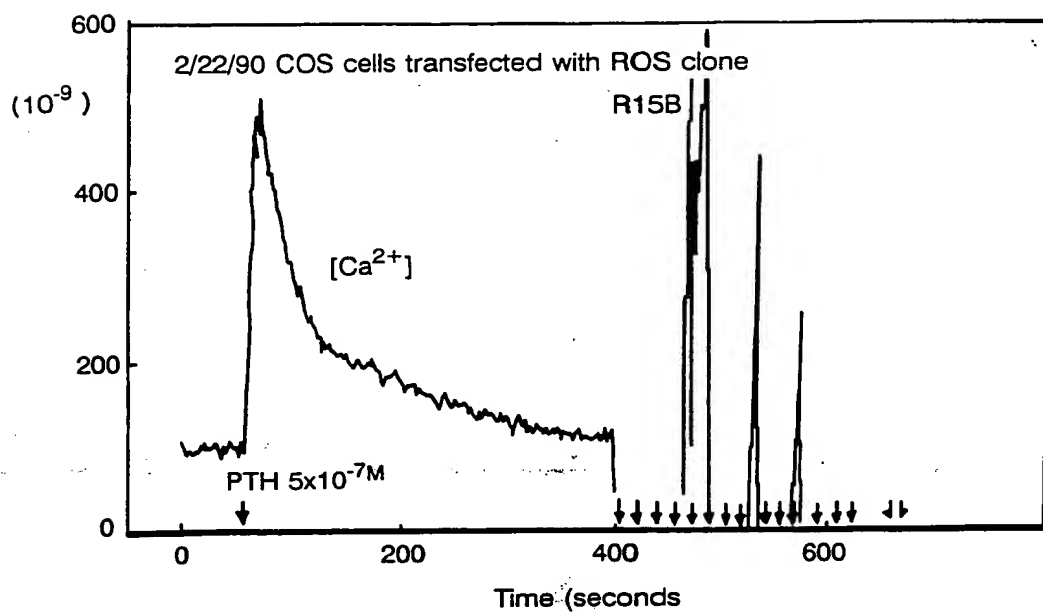


FIG. 14

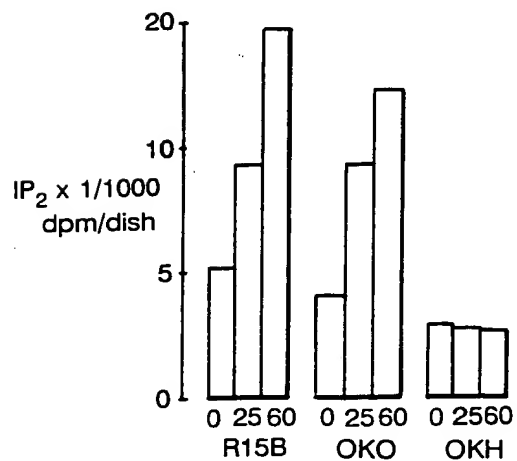


FIG. 15A

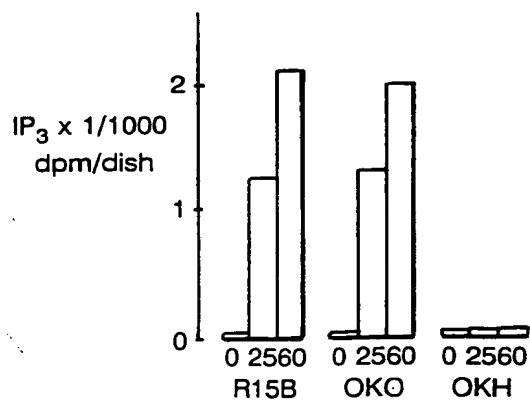
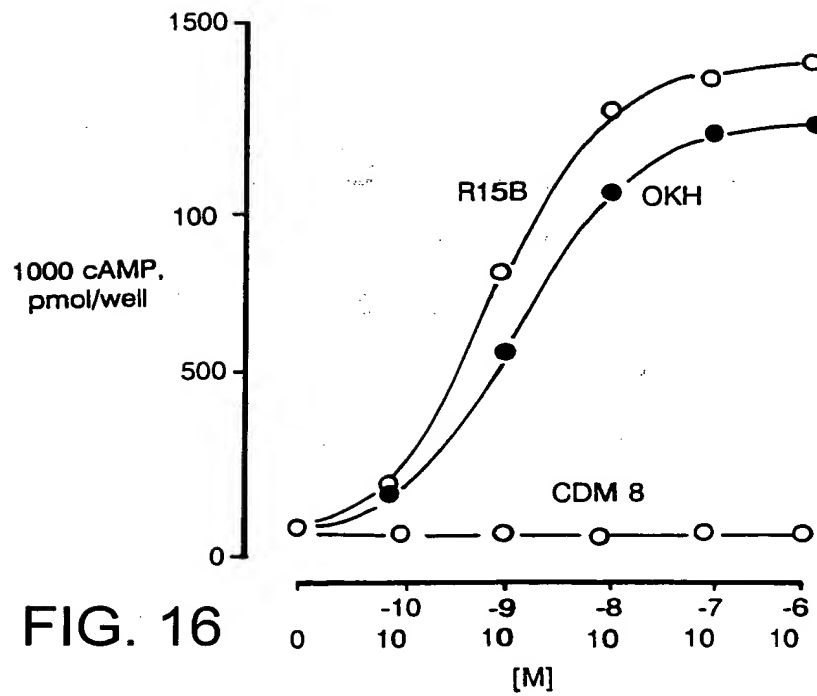


FIG. 15B



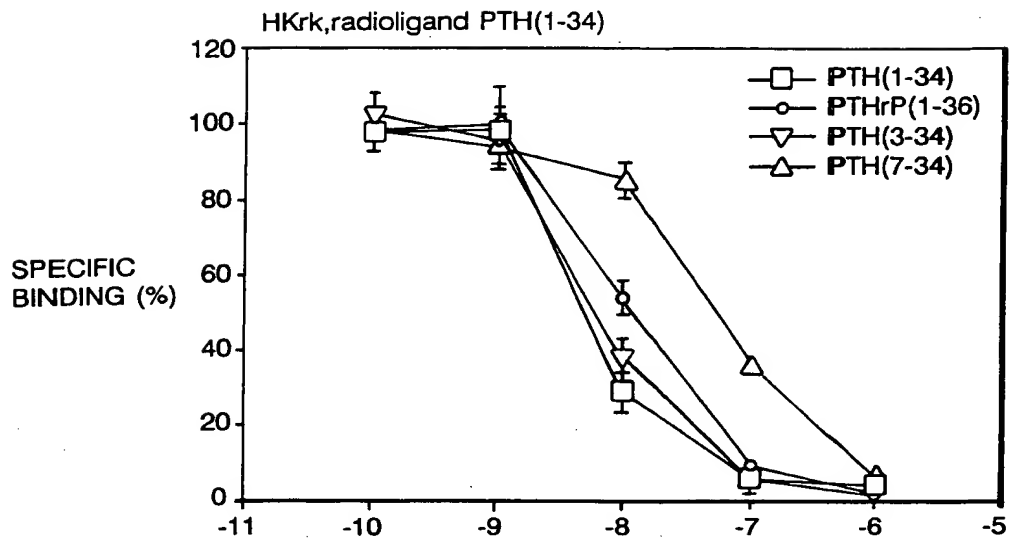


FIG. 17A

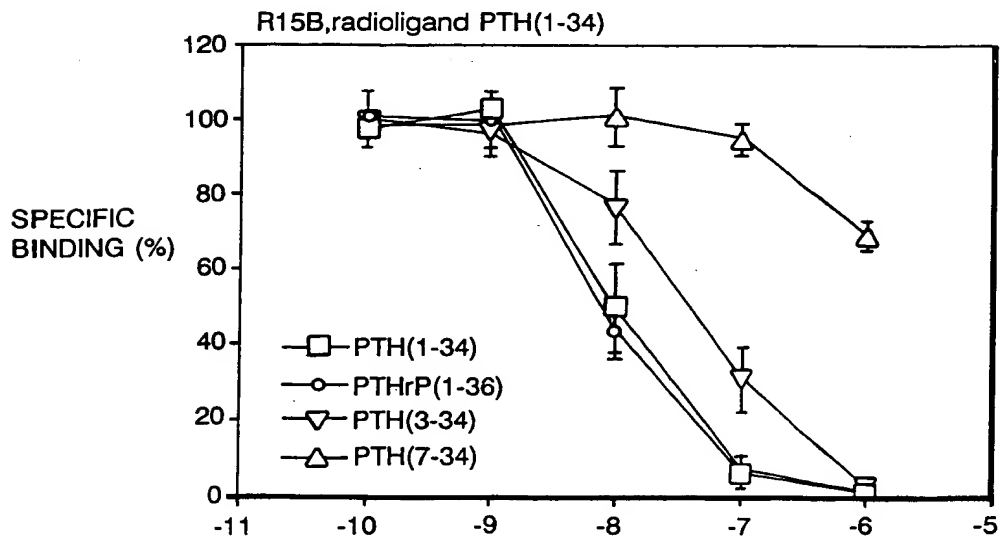


FIG. 17B



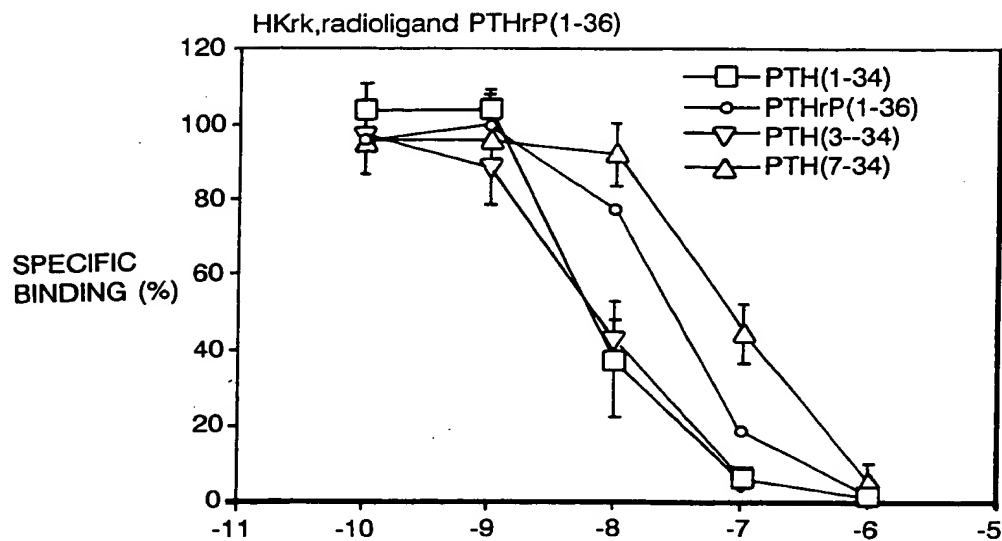


FIG. 17C

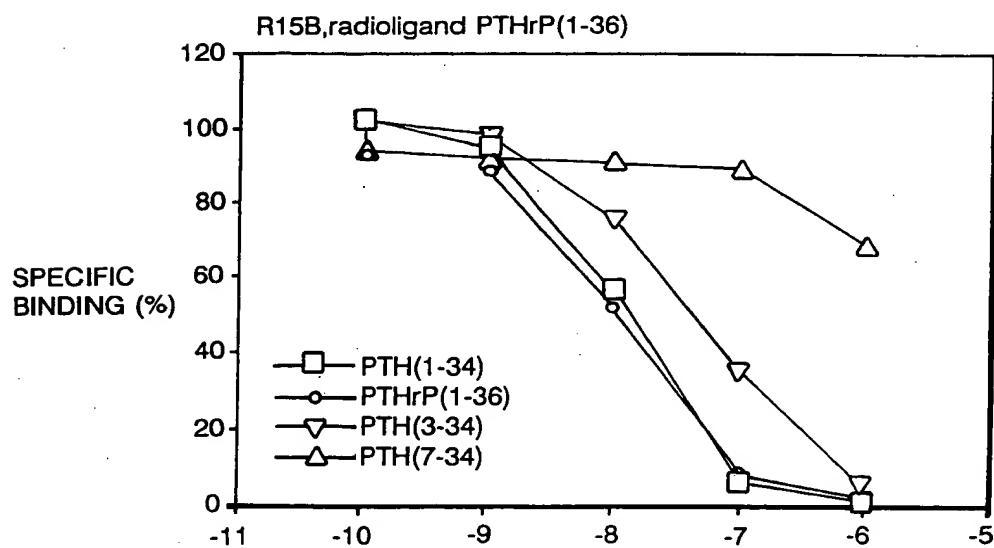


FIG. 17D

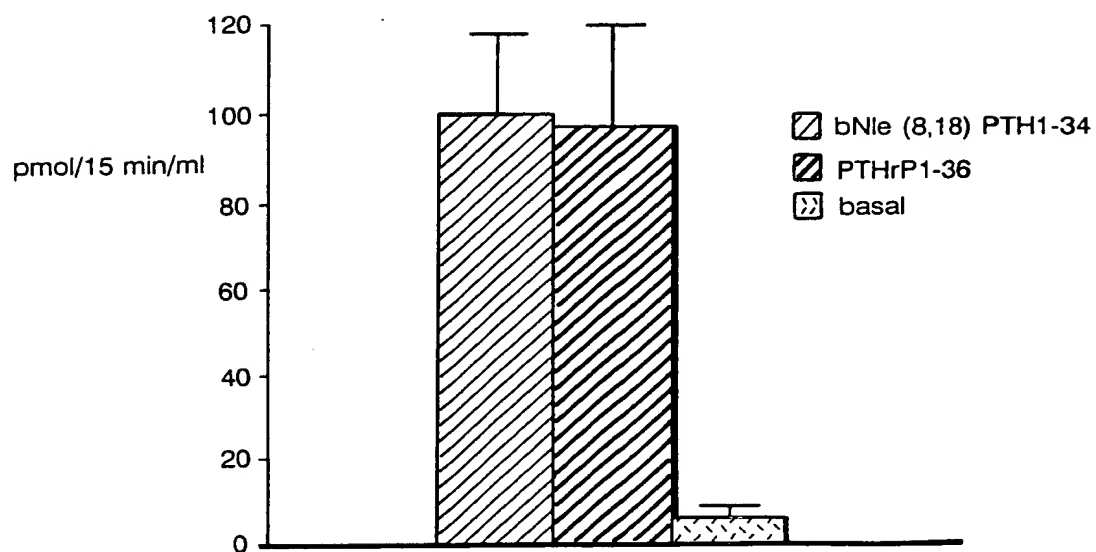


FIG. 18

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Amendment in Reply to Office action of August 5, 2004  
Replacement Sheet

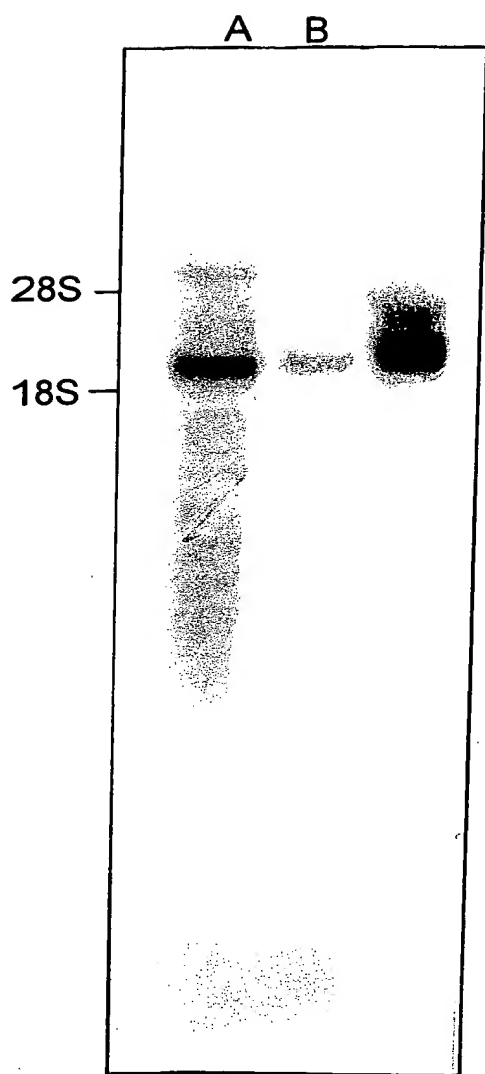


FIG. 19

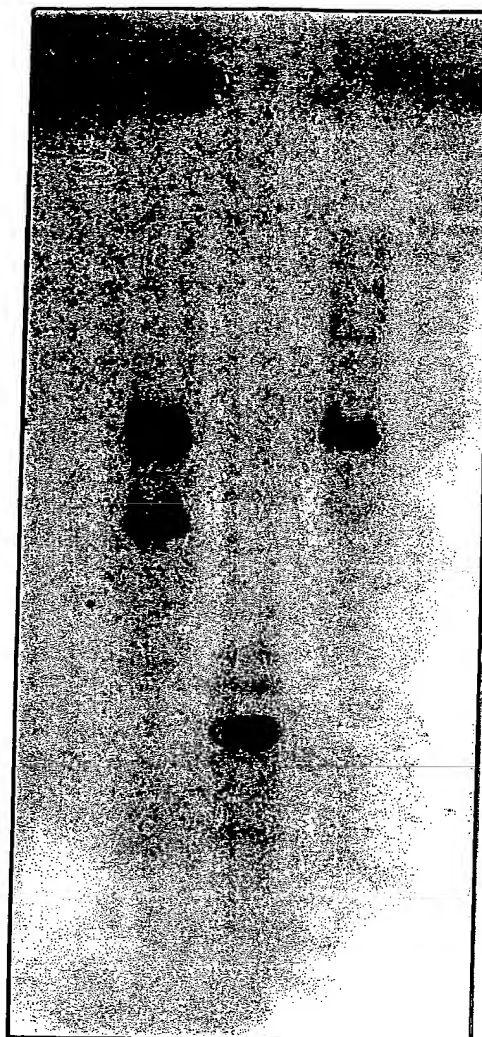
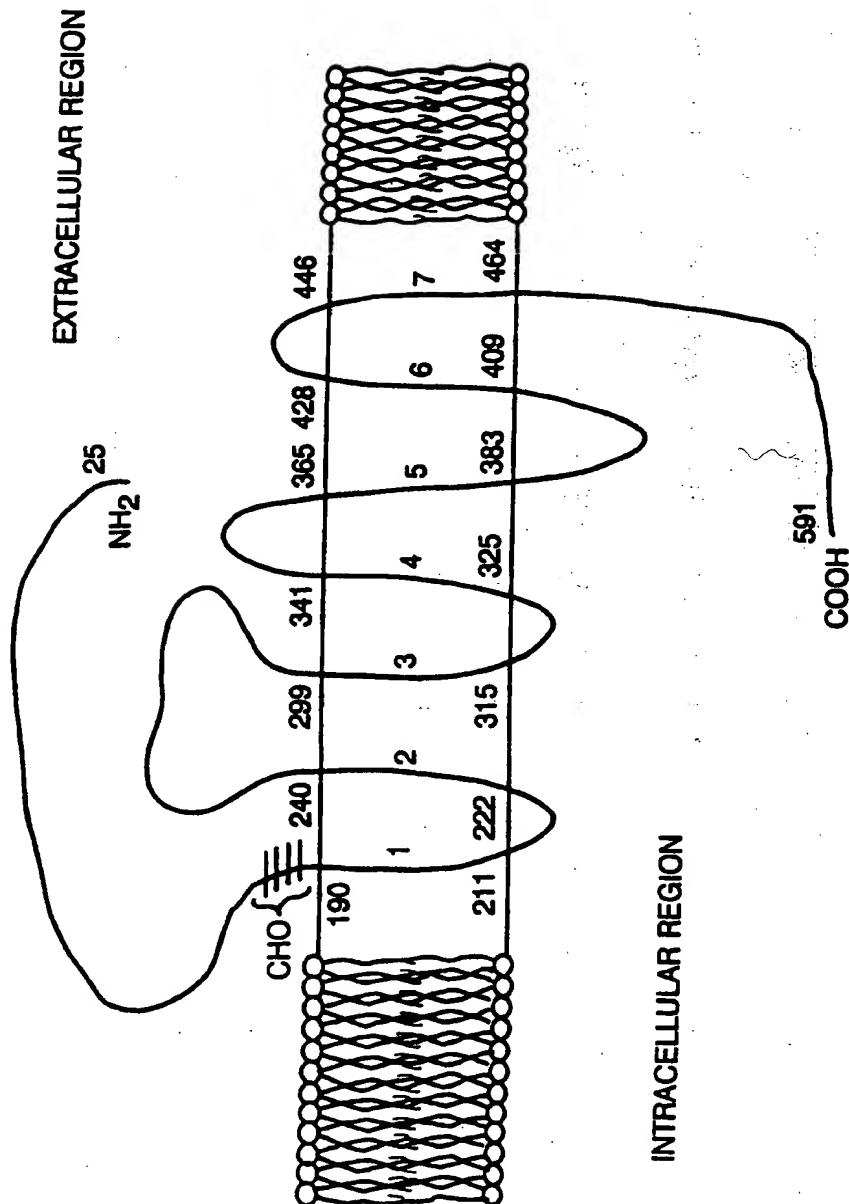


FIG. 20

# RAT BONE PTH/PTHrP RECEPTOR



## AMINO ACID SEQUENCE OF 7 PUTATIVE TRANS-MEMBRANE REGIONS

- 1 VGYSMSLASLTVAVLAY —
  - 2 IHMIMFLSFMFLRAASFVK —
  - 3 LVEGLYLSLIFMAFFS
  - 4
  - 5
  - 6 STLVLVPLFGVHYTVFMALP —
  - 7 VPILASVNLNFIINHR —
- MLFNSFQGGFFVANYCFCN

FIG. 21